DETAILED ACTION

The preliminary amendment, filed on 12 January 2010, in which claim 18 is amended to correct for the spelling of arginine, is acknowledged.

Election/Restrictions

Applicants' election without traverse of Group I, claims 1-26 and 34, drawn to an erythropoietin peptide as indicated in claim 1, in the reply filed on 12 January 2010 is acknowledged. Applicants further elect the species of (1) L-R^1 wherein L is $\{C(O)(CH_2)_aNH\}_s\{C(O)CH_2)_b(OCH_2CH_2)_cO(CH_2)_dNH\}_t$ and R_1 is $C(O)CH_2CH_2(OCH_2CH_2)_eOCH_3$, wherein s and t are independently 0 or 1, a, b, and d are independently integers from 0 to 20, and c and e are independently integers selected from 1 to 2500; and (2) asparagine as the amino acid.

The requirement is still deemed proper and is therefore made FINAL.

Claims 27-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12 January 2010.

Claims 2-5 and 10-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12 January 2010.

Claims 1, 6-9, 13-26 and 34 will be examined on its merits herein.

Priority

This application is a National Stage entry of PCT/US04/39712 filed on 24 November 2004 and claims priority to U.S. provisional application no. 60/524,989 filed on 24 November 2003, U.S. provisional application no. 60/539,387 filed on 26 January 2004, U.S. provisional application no. 60/555,504 filed on 22 March 2004, U.S. provisional application no. 60/590573 filed on 23 July 2004, U.S. provisional application no. 60/592,744 filed on 29 July 2004, U.S. provisional application no. 60/614,518 filed on 29 September 2004, and U.S. provisional application no. 60/623,387 filed on 29 October 2004.

Applicants' claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir 1994). Also see MPEP § 201.11.

The disclosure of the prior-filed applications fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The prior filed applications do not disclose an erythropoietin peptide comprising the moiety as recited in claim 1.

Thus, the priority date of the instant claims **1, 7-9, 19-26 and 34** is deemed to be the filing date of the only application that provides support for the instantly filed application, PCT/US04/39712 filed on 24 November 2004; the priority date of the instant claim **6** is deemed to be the filing date of the only provisional application that provides support for the instantly filed application, U.S. provisional application no. 60/592,744 filed on 29 July 2004; the priority date of the instant claims **13-15** is deemed to be the filing date of the only provisional application that provides support for the instantly filed application, U.S. provisional application no. 60/524,989 filed on 24 November 2003; and the priority date of the instant claims **16-18** is deemed to be the filing date of the only provisional application that provides support for the instantly filed application, U.S. provisional application no. 60/555,504 filed on 22 March 2004. If Applicant disagrees, Applicant should present a detailed analysis as to why the claimed subject matter has clear support in the earlier priority applications. Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

In clarifying the priority date of the instant claims, applicant should note or address whether the art rejections are prior to the priority date of the instant claims and whether said art occurred more than one year prior to said priority date.

Information Disclosure Statement

The information disclosure statements (IDS) dated 16 May 2006, 17 July 2006, 25 October 2007 and 3 February 2010 comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609, except where noted. Accordingly, they have been placed in the application file and the information therein has been considered as to the merits.

Non-patent literature documents by Katre *et al.*, Keppler *et al.*, Liu *et al.*, Srinivasachar *et al.*, Ulloa-Aguirre *et al.*, Witte *et al.* and Wu *et al.*, cited on the IDS dated 25 October 2007, was not considered because the documents were each missing the first page of the journal citation. The missing page could not be found in the documents submitted before or after this citation and the number of pages received by the Office as shown in PALM corresponds to the number of pages noted on the EFS acknowledgement receipt. With the exception of the Liu *et al.* citation, full copies of these documents were re-submitted on the IDS dated 3 February 2010 and have been considered.

Non-patent literature documents by Takeda *et al.* and Wang *et al.* cited on the IDS dated 25 October 2007 were not considered because the first page of each document was not readable.

Non-patent literature document by Abuchowski (p. 3582-3586) cited on the IDS dated 25 October 2007 was not considered because a copy of the document was not provided to the Office with the IDS. This document was submitted on the IDS dated 3 February 2010 and has been considered.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below:

The disclosures of SEQ ID No. 1 and 2 must be submitted as a separate part of the disclosure, a paper or compact disc copy (see § 1.52(e)) disclosing the nucleotide and/or amino acid sequences and associated information using the symbols and format in accordance with the requirements of §§ 1.822 and 1.823.

The Specification is objected to because the subject matter of originally filed instant claim 19 is not adequately described in the Specification. Specifically, there is no disclosure in the Specification of a compound having the third structure as shown in the claim wherein the variable "G" is further connected to the variable "R^1" of the lowest branch. Applicants are requested to amend the Specification to include the instantly claimed subject matter. See MPEP § 608.01(l).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Section [0001]

Claims 1, 6-9, 13-26 and 34 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by WO 03/031464 to DeFrees *et al.* (of record).

DeFrees *et al.* disclose methods and compositions for remodeling a peptide molecule, including the addition or deletion of one or more glycosyl groups to the peptide, and/or the addition of a modifying group to the peptide. Modifying groups include water-soluble polymers, such as poly(ethylene glycol) (p. 152, lines 7-25 WIPO). The use of poly(ethylene glycol) to derivatize peptide therapeutics has been demonstrated to reduce the immunogenicity of the peptides and prolong their clearance time from circulation (p. 4, lines 3-9). The PEG moiety has been shown to be attached via a peptide amino acid residue (p. 4, lines 13-20) or an oxidized glycosyl residue of the peptide (p. 4, line 28 – p. 5). DeFrees *et al.* disclose an *in vitro* method for the modification of erythropoietin (EPO), wherein the peptide has the formula $-AA-X^1-X^2$ (p. 9, lines 12-26) or formula $-AA-(X^1)_n$. More specific structures of the X^1-X^2 glycosyl residues are shown on p. 13-15. DeFrees *et al.* further disclose a pharmaceutical composition comprising a pharmaceutically acceptable diluent and a covalent conjugate between a polymer and a glycosylated or non-glycosylated peptide, wherein the polymer is conjugated to the peptide via an intact glycosyl linking group interposed

between and covalently linked to both the peptide and the polymer (p. 21, lines 9-12). In one embodiment, a conjugate is formed between EPO and a modifying group, wherein the modifying group is covalently attached to the EPO peptide through an intact glycosyl linking group, and the EPO peptide comprises a glycosyl residue having a formula as indicated (p. 37, line 26 - p. 38, line 21). The modifying group exemplified in the disclosure of DeFrees *et al.* is poly(ethylene glycol) molecules, such as those in formula 3 (p. 154, line 28 – p. 156). The PEG molecules disclosed on p. 156 meet the limitations of the R^1 structure of the instant claims. Scheme 3 discloses a modified glycoPEG-ylated compound, such as albumin-PEG-SA-EPO, wherein EPO represents erythropoietin and SA represents sialic acid, which can be used in a method for extending the blood-circulation half-life of selected peptides (p. 149, Scheme 3 and lines 1-10). Formula 1 discloses the structure of a remodeled N-linked glycan, comprising a tri-mannosyl core, preferably linked to an asparagine residue on a peptide backbone (p. 129, lines 10-21). When expressed in CHO cells, the N-linked glycans will have the structures as depicted in the top row of Figure 3, which meets the structure limitations of claim 16 (p. 131, line 30 – p. 132, line 19). When expressed in insect cells, the N-linked glycans will have the structures as depicted in Figure 7, which meets the structure limitations of claim 13 (p. 132, line 20 - p. 133, line 15). When expressed in yeast cells, the N-linked glycan will have a structure as depicted Figure 5 (p. 133, lines 16-24). Additionally, Figure 9 depicts well-known strategies for the synthesis of biantennary, triantennary and even tetraantennary glycan structures beginning with the trimannosyl core structure, which meets the structure limitations of claims 19 and 20. Methods for

the modification of O-linked glycans wherein the peptide is modified with a GalNAc donor, followed by Gal and SA via the use of appropriate glycosyltransferases is also disclosed (p. 140, lines 20-28). The modifying group can be attached to sialic acid at either the 9-position on the pyruvyl side chain or at the 5-position on the amine moiety of sialic acid (p. 150, lines 5-11). The preparation of CMP-SA-PEG, wherein PEG is attached to the C5 position, is disclosed in Scheme 4 (p. 177) and further exemplified in Example 8 (p. 348, line 4 – p. 351, line 21). Table 2 also discloses CMP-SA compounds wherein the glycerol side chain is modified with PEG, such as on the 9-position (p. 178). Preparation of the 9-modified CMP-SA compound is disclosed in Scheme 8 (p. 181). Example 19 discloses a method for N-linked glycoPEGylation of EPO produced in insect cells with CMP-SA-PEG (p. 362, line 8 – p. 364, line 4). The methods are further schematically represented in Figure 33 which discloses the modification of the glycan structure on EPO with PEG (p. 85, lines 8-13). Additionally, Figure 33A shows that N-linked glycosylation occurs as positions 24, 38 and 83 of the peptide backbone (p. 108). Figure 58 discloses exemplary nucleotide and corresponding amino acid sequences of EPO as SEQ ID Nos 15 and 16, respectively (p. 92, lines 17-19). SEQ ID No. 16 has the same sequence as SEQ ID No. 1 of the instant claims. Figure 126 discloses the results of an *in vitro* bioassay comparing PEGylated EPO with non-PEGylated EPO (p. 99, lines 22-25). EPO glycoPEGylated with 1 kDa PEG had almost the same activity as the unglycoPEGylated EPO when both were at a concentration of approximately 5 μg/mL. The EPO glycoPEGylated with 10

kDa PEG had approximately half the activity of the unglycoPEGylated EPO when both were at a concentration of approximately 5 μg/mL (p. 363, line 30 - p. 364, line 4).

It is noted that DeFrees *et al.* do not expressly teach that PEGylated EPO is tissue protective or essentially non-erythropoietically active, as recited in the instant claims. However, the recitations "is essentially non-erythropoietically active" and "is tissue protective" are considered to be a result of the structural claim limitations. Thus, Applicants' recitations are not considered to further limit the claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount, as the instantly claimed. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See also MPEP § 2112.01.

Thus, the disclosure of a glycoPEGylated EPO, as well as methods for the preparation of said structure, disclosed by DeFrees *et al.*, anticipates claims 1, 6-9, 13-26 and 34.

Section [0002]

Claims 1, 6-9, 13-26 and 34 are rejected under 35 U.S.C. 102(e) as being anticipated by PG Pub No. US 2007/0042458 A1 to DeFrees *et al.* (of record), as

evidenced by journal publications by Kawasaki *et al.* (PTO-892, Ref. V) Sasaki *et al.* (PTO-892, Ref. W).

DeFrees *et al.* disclose methods and compositions for remodeling a peptide molecule, including the addition or deletion of one or more glycosyl groups to the peptide, and/or the addition of a modifying group to the peptide. Modifying groups include water-soluble polymers, such as poly(ethylene glycol) (paragraphs 0655-0657). The use of poly(ethylene glycol) to derivatize peptide therapeutics has been demonstrated to reduce the immunogenicity of the peptides and prolong their clearance time from circulation (paragraph 0011). The PEG moiety has been shown to be attached via a peptide amino acid residue (paragraph 0013) or an oxidized glycosyl residue of the peptide (paragraph 0014). DeFrees *et al.* disclose an *in vitro* method for the modification of erythropoietin (EPO), wherein the peptide has the formula $-AA-X^1-X^2$ (paragraph 0031) or formula $-AA-(X^1)_n$. More specific structures of the X^1-X^2 glycosyl residues are shown in paragraph [0067], paragraph [0082], paragraph [0088], paragraph [0090] and paragraph [0114]. DeFrees *et al.* further disclose a pharmaceutical composition comprising a pharmaceutically acceptable diluent and a covalent conjugate between a polymer and a glycosylated or non-glycosylated peptide, wherein the polymer is conjugated to the peptide via an intact glycosyl linking group interposed between and covalently linked to both the peptide and the polymer (paragraph 1340). In one embodiment, a conjugate is formed between EPO and a modifying group, wherein the modifying group is covalently attached to the EPO peptide through an intact glycosyl linking group, and the EPO peptide comprises a glycosyl

residue having a formula as indicated (paragraphs 0114-0120). The modifying group can be attached to sialic acid at either the 9-position on the pyruvyl side chain or at the 5-position on the amine moiety of sialic acid (paragraph 0647). Exemplary modifying groups include PEG compounds having the structures as shown in paragraph 0672. DeFrees *et al.* further teach that the reactive functional groups between the sugar moiety and the modifying group can include such functional groups as amines and carboxyl groups (paragraphs 0753, 0754, and 0760). Scheme 3 discloses a modified glycoPEG-ylated compound, such as albumin-PEG-SA-EPO, wherein EPO represents erythropoietin and SA represents sialic acid, which can be used in a method for extending the blood-circulation half-life of selected peptide (paragraph 0643). Figure 10 discloses a scheme depicting two *in vitro* strategies for the synthesis of monoantennary glycans, and the optional glycoPEGylation of the structures. EPO having monoantennary PEGylated glycan structures is prepared by expressing EPO peptide in insect cells (paragraph 1509). These structures meet the limitations of claim 13. Additionally, Figure 11 depicts well-known strategies for the synthesis of biantennary, triantennary and even tetraantennary glycan structures beginning with the trimannosyl core structure. The methods for obtaining bi-antennary branching and tri-antennary branching of EPO glycans is further exemplified in paragraphs 1528-1547). Example 13 discloses a method for N-linked glycoPEGylation of EPO produced in insect cells with CMP-SA-PEG (paragraphs 1481-1492) and Example 14 discloses a method for the glycoPEGylation of EPO produced in CHO cells (paragraphs 1493-1494). As evidenced by Kawasaki *et al.* and Sasaki *et al.*, the glycosyl moieties obtained from

EPO produced in CHO cells have structures that meet the limitations of claims 16, 19 and 20. The preparation of CMP-SA-PEG, wherein PEG is attached to the C5 position, is disclosed in Scheme 4 (p. 84) and further exemplified in Examples 1 and 2 (paragraphs 1359-1374). Table 3 also discloses CMP-SA compounds wherein the glycerol side chain is modified with PEG, such as on the 8- and 9-positions (p. 84-85). Preparation of the 9-modified CMP-SA compound is disclosed in Schemes 7 and 8 (p. 87-88). The methods are further schematically represented in Figure 35 which discloses the modification of the glycan structure on EPO with PEG (paragraph 0220). Additionally, Figure 33A shows that N-linked glycosylation occurs as positions 24, 38 and 83 of the peptide backbone. Figure 64 discloses exemplary nucleotide and corresponding amino acid sequences of EPO as SEQ ID Nos 15 and 16, respectively (paragraph 0249). SEQ ID No. 16 has the same sequence as SEQ ID No. 1 of the instant claims. Figure 130 discloses the results of an *in vitro* bioassay comparing PEGylated EPO with non-PEGylated EPO (paragraph 0315).

It is noted that DeFrees *et al.* do not expressly teach that PEGylated EPO is tissue protective or essentially non-erythropoietically active, as recited in the instant claims. However, the recitations "is essentially non-erythropoietically active" and "is tissue protective" are considered to be a result of the structural claim limitations. Thus, Applicants' recitations are not considered to further limit the claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount, as the instantly claimed. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161.

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See also MPEP § 2112.01.

Thus, the disclosure of a glycoPEGylated EPO, as well as methods for the preparation of said structure, disclosed by DeFrees *et al.*, anticipates claims 1, 6-9, 13-26 and 34.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6-8, 16-26 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0605963 A2 to Wright (of record), as evidenced by WIPO publication WO 01/76640 to Kinstler *et al.* (PTO-892, Ref. N), in view of PG Pub No. US 2002/0016003 to Saxon *et al.* (PTO-892, Ref. A), in view of journal publication by Lin *et al.* (PTO-892, Ref. U), as evidenced by journal publications by Kawasaki *et al.* (PTO-892, Ref. V) and Sasaki *et al.* (PTO-892, Ref. W).

Wright teaches methods and compounds for modifying polypeptides with PEG or other water-soluble organic polymers. Protein and other similar organic molecules are chemically modified by covalent conjugation to water-soluble organic polymers, such as PEG, because of the desirable properties conferred on the polypeptides by attachment of the water-soluble polymers. The desirable properties include solubility in aqueous solutions, increased stability during storage, reduced immunogenicity, increased resistance to enzymatic degradation, compatibility with a wider variety of drug administration systems, and increased *in vivo* half-life (p. 2, lines 11-16). Erythropoietin (EPO) is a glycoprotein which regulates red blood cell production. It consists of 165

amino acids, and has four carbohydrate chains emanating from the protein backbone, three N-linked at N24, N38 and N83, and one O-linked at S126. The carbohydrate groups on EPO are believed to increase the solubility of EPO and prolong its serum half-life (p. 3, lines 19-26). Conjugation of mPEG to a cysteine residue of EPO is known (p. 3, lines 5-9). However, Wright teaches that it may be advantageous to couple water-soluble reagents to the carbohydrate moiety of a glycoprotein rather than to the polypeptide backbone amino acids because of differences in charge displacement, steric hinderance, amino acid residues at active sites, and other problems that may disrupt the structure and function of the polypeptide component of the water-soluble polymer modified glycoproteins (p. 3, lines 38-46). By providing for water-soluble polymer reagents that may be coupled to the carbohydrate moiety of glycoproteins it may be possible to covalently conjugate water-soluble polymers to proteins without substantially adversely affecting the biological activity of proteins that would be adversely affected through coupling at other amino acid residues (p. 3, lines 47-50). Wright teaches that hydrazine and oxylamine derivatives of water-soluble polymers, such as PEG, may be covalently attached to proteins through reactions with aldehyde groups or other suitable functional groups present on the protein of interest (p. 7, lines 5-11). Aldehyde groups may be introduced by partially oxidizing the hydroxyl groups on the polypeptide, such as hydroxyl groups present on the carbohydrate moieties of the polypeptide, with galactose oxidase or periodate (p. 7, lines 11-16). Hydrazide and oxylamine derivatives are further disclosed (p. 7, lines 19-58). Examples of PEG water soluble polymers include polyethylene glycol, methoxypolyethylene glycol, polyethylene

glycol homopolymers, polypropylene glycol homopolymers, copolymers of ethylene glycol with propylene glycol (p. 7, line 58 – p. 8, line 3). Wright further teaches that the disclosed preparation may be administered alone or in an admixture with a pharmaceutical carrier or diluent selected with regard to the intended route of administration and standard pharmaceutical practice (p. 12, lines 14-21). Methods for the synthesis of mPEG-hydrazide from mPEG-OH (p. 12, line 55 - p. 13, line 37) and mPEG-semicarbazide from mPEG-NH_2 (p. 13, line 50 – p. 14, line 16) are further disclosed. Additionally, methods for the modification of EPO with mPEG-hydrazide and mPEG-semicarbazide are further disclosed wherein EPO is oxidized with sodium periodate followed by conjugation of the resulting aldehyde with PEG (p. 18, line 26 - p. 19, line 14). It is noted that Wright does not expressly teach which carbohydrate group is oxidized to an aldehyde in the presence of sodium periodate. However, as evidenced by Kinstler *et al.*, 10 mM sodium periodate oxidation of EPO targets the pendant diol of the penultimate glycosyl unit sialic aicd residue (p. 11, lines 1-10 and p. 19, lines 29-33).

The teachings of Wright differ from that of the instantly claimed invention in that Wright does not expressly teach conjugation of the PEG polymer to the 9-position or 5-position of sialic acid, as recited in the instant claims.

Saxon *et al.* teach a method for covalent modification of molecules. The chemoselective ligation reaction can be carried out under physiological conditions, and involves condensation of a specifically engineered phosphine, which can provide for formation of an amide bond between the two reactive partners resulting in a final product comprising a phosphine oxide, or which can be engineered to comprise a

cleavable linker so that a substituent of the phosphine is transferred to the azide of the other molecule (paragraph 0018). The selectivity of the reaction and its compatibility with aqueous environments provides for its application *in vivo* and *in vitro*, e.g. synthesis of peptides and other polymers. Saxon *et al.* disclose the use of a synthetic substrate comprising an abiotic reactive partner, such as the azido compounds of paragraphs 0067-0070, for incorporation into a biopolymer, which is utilized in the glycoprotein biosynthetic pathway. For example, host cells provided with synthetic sialic acid azido-derivatives, such as those disclosed in paragraphs 0067-0070, incorporates these compounds into the sialic acid biosynthetic pathway, eventually resulting in the incorporation and expression of the synthetic sugar residues on glycoproteins (paragraph 0066). The azido-modified glycoprotein can then undergo a chemoselective ligation reaction with another molecule engineered with a phosphine. The engineered phosphine can be modified to comprise a molecule desired for delivery and conjugation to the azido-target substrate, such as that comprising detectable labels, small molecule drugs, cytotoxic molecules, ligands for binding by a target receptor, tags to aid in purification, and molecules to facilitate selective attachment of the polypeptide to a surface (paragraph 0075). The chemoselective ligation can be performed with a modified phosphine that comprises a cleavable linker. Thus, reaction of i) a first reactant comprising a first molecule of interest engineered with a phosphine comprising a cleavable linker, with ii) a second reactant comprising a second molecule of interest engineered with an azide, results in conjugation of the first molecule of interest to the second molecule of interest via an amide or a thioamide bond, accompanied by the

release of nitrogen and an oxidized phosphine byproduct (paragraph 0109). This reaction is further schematically illustrated in paragraph 0109. As shown in Example 6, cells incorporate N-azidoacetylmannosamine into cell surface glycans, as detected by labeling of the cells with biotin modified with a phosphine group, followed by FITC-avidin staining (paragraph 0198). Example 7 illustrates a method wherein two peptides, one modified with an azido group, and the other modified with a phosphine group with a cleavable linker, are conjugated together to form an amide bond between the two peptides. Saxon *et al.* further disclose that previous work showed that incorporation of a ketone-bearing group, such as a levulinoyl group, can be expressed on glycoproteins as SiaLev, and that the ketone group on SiaLev can be chemoselectively conjugated to compounds or other molecules bearing a hydrazide group (paragraphs 0008-0010).

Lin *et al.* teach a method for cloning and expression of the human erythropoietin gene. The sequence of the clone is shown in Figure 3 (p. 7583) and is the same as SEQ ID No. 2, which encompasses the sequence of SEQ ID No. 1. Introduction of the clone into Chinese hamster ovary (CHO) cells produces erythropoietin that is biologically active *in vitro* and *in vivo* (abstract). As evidenced by Kawasaki *et al.* (Table 1) and Sasaki *et al.* (Table III), CHO cells produce EPO glycans that have the same core structures as that of instant claims 16, 19 and 20.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Wright, concerning the modification of peptides, such as EPO, with water-soluble polymers, such as PEG, with the teachings of Saxon *et al.*, regarding chemoselective ligations involving a ketone group with a hydrazide

group, or an azido group with a phosphine, with the teachings of Lin *et al.*, regarding the cloning of human EPO and its expression in CHO cells. Since Wright teaches that water-soluble polymers, such as PEG-hydrazide derivatives, can be conjugated to the carbohydrate moieties of glycoproteins, such as EPO, which have been oxidized to an aldehyde group or other suitable functional group, one of ordinary skill in the art would have been motivated to conjugate the PEG-hydrazide derivatives onto glycoproteins expressing a ketone group, such as that present on SiaLev, as disclosed by Saxon *et al.* Since Saxon *et al.* teach that biotin-hydrazide can be selectively conjugated to the ketone group of SiaLev, which is expressed on the terminus of a glycoprotein, one of ordinary skill in the art would reasonably expect that substitution of biotin-hydrazide with PEG-hydrazide would yield a predictable result. With regards to obtaining EPO containing a terminal SiaLev group on its glycans, Lin *et al.* teach the expression of rhEPO in a CHO system. Thus, based on the combined teachings of Saxon *et al.* and Lin *et al.*, one of ordinary skill in the art would reasonably expect that expression of EPO in the CHO system in the presence of a SiaLev as disclosed by Saxon *et al.*, would predictably yield EPO modified with SiaLev on its glycans. Moreover, as Saxon *et al.* teach that azido groups can be introduced onto sialic acids present on glycoproteins using a similar method to that of SiaLev, and that the azido groups chemoselectively react with phosphine groups, one of ordinary skill in the art would have been motivated to modify the PEG-hydrazide compounds, disclosed by Wright, into PEG-phosphine compounds for conjugation to azido groups introduced onto the sialic acid residue of glycoproteins. One of ordinary skill in the art would have been motivated to select the

azide-phosphine chemistry, in order to receive the expected benefit, as disclosed by Saxon *et al.*, that these two groups are abiotic to cell surfaces. One of ordinary skill in the art would have been motivated to conjugate PEG onto EPO, in order to receive the expected benefit, as disclosed by Wright, that conjugation of PEG to a peptide increases its solubility in aqueous solutions, stability during storage, and resistance to enzymatic degradation, and reduces its immunogenicity, as well as increasing its *in vivo* half-life. Moreover, as disclosed by Wright, it may be advantageous to couple PEG to the carbohydrate moiety of a glycoprotein rather than to the polypeptide backbone amino acids because of differences in charge displacement, steric hinderance, amino acid residues at active sites, and other problems that may disrupt the structure and function of the polypeptide component of the water-soluble polymer modified glycoproteins. Thus, although Saxon *et al.* exemplify conjugation of a hydrazide or phosphine group onto sialic acid derivatives expressed on glycoproteins as a detection method, Saxon *et al.* do disclose that small molecules, peptide, ligands, etc., could be conjugated to the azido or ketone group introduced onto sialic acid. As such, in view of the teachings of Wright, it would have been *prima facie* obvious to one of ordinary skill in the art that other molecules could be conjugated to the sialic acid derivatives present on the glycoproteins.

It is noted that DeFrees *et al.* do not expressly teach that PEGylated EPO is tissue protective or essentially non-erythropoietically active, as recited in the instant claims. However, the recitations "is essentially non-erythropoietically active" and "is tissue protective" are considered to be a result of the structural claim limitations. Thus,

Applicants' recitations are not considered to further limit the claims drawn to a composition or product, so long as the prior art discloses the same composition comprising the same ingredients in an effective amount, as the instantly claimed. See, e.g., *Ex parte Masham*, 2 USPQ2d 1647 (1987) and *In re Hack* 114, USPQ 161. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See also MPEP § 2112.01.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Statutory Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1, 6-9, 13, 16, 19, 20, 23-26 and 34 of this application conflict with claims 35, 40, 46-56 and 61 of Application No. 11/981,483. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one

application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

Obviousness-Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 86-107 of copending U.S. application no. 12/444,380.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a method of making a composition comprising a first polypeptide conjugate, wherein said first polypeptide conjugate comprises a first number of poly(alkylene oxide) moieties covalently linked to said first polypeptide. The first polypeptide conjugate is EPO (claim 13). The EPO is linked to PEG via an N-linked glycan (claim 15). Claim 74 is drawn to a pharmaceutical composition comprising the isolated polypeptide conjugate and a pharmaceutically

acceptable carrier. The copending application is also drawn to a method of treating various conditions comprising administering the composition according to claim 75. Claim 102 indicates that the glycosyl linking moiety may be selected from a group that includes sialic acid. The Specification further defines the PEGylated sialic acid structure.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6 and 34 are seen to be obvious over claims 86-107 of copending U.S. application no. 12/444,380.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending U.S. application no. 12/496,595.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a covalent conjugate between a peptide and a water soluble polymer, wherein said water soluble polymer is not a naturally occurring sugar and is covalently attached to said peptide through an

intact glycosyl linking group. The water soluble polymer is PEG (claims 2-7). The water soluble polymer is attached to sialic acid at the 5- or 9-poisition (claim 12). The peptide is selected from a group that includes erythropoietin (claim 14). The claims are also drawn to a pharmaceutical composition comprising the covalent conjugate according to claim 1 and a pharmaceutically acceptable diluent (claim 15). The claims are further drawn to a method of forming the covalent conjugate.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1 and 34 are seen to be obvious over claims 1-4 of copending U.S. application no. 12/496,595.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending U.S. application no. 12/443,428.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a peptide conjugate comprising a peptide which is covalently attached to a moiety which is a member

selected from the group as shown in claim 1. Claim 3 defines the PEGylated structures on sialic acid. The peptide is selected from a group that includes erythropoietin (claim 4).

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1 and 34 are seen to be obvious over claims 1-4 of copending U.S. application no. 12/443,428.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 86-107 of copending U.S. application no. 12/418,530.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a method of making a composition comprising a first polypeptide conjugate, wherein said first polypeptide conjugate comprises a first number of poly(alkylene oxide) moieties covalently linked to said first polypeptide. The first polypeptide conjugate is EPO (claims 86 and 90). Claim 102 indicates that the glycosyl linking moiety may be selected from a group that

includes sialic acid. The Specification further defines the PEGylated sialic acid structure.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6 and 34 are seen to be obvious over claims 86-107 of copending U.S. application no. 12/418,530.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 12 and 15-19 of copending U.S. application no. 12/152,587.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a polypeptide conjugate comprising the structure as shown in formula **(I)**. Claim 2 indicates that the peptide may be erythropoietin. Claim 12 indicates that the polymeric moiety is poly(ethylene glycol). Claim 17 shows the glycosyl moiety as having a sialic acid structure. The structure of PEG is further defined in claim 18.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6 and 34 are seen to be obvious over claims 1, 2, 12 and 15-19 of copending U.S. application no. 12/152,587.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3-6, 9-26 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 47-78 of copending U.S. application no. 11/982,273.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to an erythropoietin peptide comprising a glycosyl linking group covalently linked to an amino acid residue of said peptide, said glycosyl linking group comprising a modified sialyl residue comprising the formula of claim 47. Claims 48-50 and 54 and 55 further limit the structures of the glycosyl linking group. Claim 63 is drawn to a pharmaceutical formulation comprising an EPO peptide according to claim 47, and a pharmaceutically acceptable carrier. The dependent claims also limit the EPO peptide to SEQ ID NO:1, and the site of glycosylation to asparagine residues 24, 38 and 83.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 3-6, 9-26 and 34 are seen to be obvious over claims 47-78 of copending U.S. application no. 11/982,273.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 14, 15, 17, 18, 21 and 22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 41-45 of copending U.S. application no. 11/981,483.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to an erythropoietin peptide conjugate comprising a sialic acid moiety as shown in the formula of claim 35. Claims 41-45 further limit the EPO peptide to SEQ ID NO:1, and the site of glycosylation to asparagine residues 24, 38 and 83.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan

structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 14, 15, 17, 18, 21 and 22 are seen to be obvious over claims 41-45 of copending U.S. application no. 11/981,483.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10, 16, 19 and 21 of copending U.S. application no. 11/781,885.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a polypeptide conjugate comprising the structure as shown in formula (V). Claim 19 indicates that the peptide may be selected from a group that includes erythropoietin. Claim 16 indicates that the polymeric moiety is poly(ethylene glycol). Claim 21 indicates that the polymeric moiety is attached via the sugar residue denoted as formula (VII).

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limit the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1 and 6 are seen to be obvious over claims 10, 16, 19 and 21 of copending U.S. application no. 11/781,885.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13, 20, 23 and 26 of copending U.S. application no. 11/781,900.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a polypeptide conjugate comprising the structure as shown in formula (V). Claim 23 indicates that the peptide may be selected from a group that includes erythropoietin. Claim 20 indicates that the polymeric moiety is poly(ethylene glycol). Claim 26 indicates that the polymeric moiety is attached via the sugar residue denoted as formula (VII).

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1 and 6 are seen to be obvious over claims 13, 20, 23 and 26 of copending U.S. application no. 11/781,900.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 6 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 5, 6, 10, 15, 16, 19, 21 and 22 of copending U.S. application no. 11/781,888.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a generic polypeptide conjugate as defined in claim 1, as well as a polypeptide conjugate comprising the structure as shown in formula (V). Claims 6 and 19 indicate that the peptide may be selected from a group that includes erythropoietin. Claims 3, 5 and 16 indicate that the polymeric moiety is poly(ethylene glycol) that is linear or branched, with structures as defined in said claims. Claims 5 and 21 indicate that the polymeric moiety is attached via the sugar residue denoted as formulas (III) or (VII).

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1 and 6 are seen to be obvious over claims 1, 3, 5, 6, 10, 15, 16, 19, 21 and 22 of copending U.S. application no. 11/781,888.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27, 32, 38 and 39 of copending U.S. application no. 11/866,969.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a method of isolating a first polypeptide conjugate comprising a first number of PEG moieties covalently linked to said first polypeptide, from a second polypeptide conjugate comprising a second number of PEG moieties covalently linked to said second polypeptide. Claim 32 indicates that the peptide may be selected from a group that includes erythropoietin. Claims 38 and 39 indicate that the PEG moiety is attached to the polypeptide via a glycosyl linking group. Although not recited in the claims, the claimed invention encompasses EPO-SA-PEG, as disclosed in the Specification.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claim 1 is seen to be obvious over claims 27, 32, 38 and 39 of copending U.S. application no. 11/866,969.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 10, 23 and 26-28 of copending U.S. application no. 11/781,896.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a generic polypeptide conjugate as defined in claim 1. Claims 8 and 23 indicate that the peptide may be selected from a group that includes erythropoietin. Claims 3, 4, 7 and 27 indicate that the polymeric moiety is poly(ethylene glycol) that is linear or branched, with structures as defined in said claims. Claims 7 and 26 indicate that the polymeric moiety is attached via the sugar residue denoted as formulas (III) or (VII).

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limit the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6 and 34 are seen to be obvious over claims 1-8, 10, 23 and 26-28 of copending U.S. application no. 11/781,896.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 10, 23 and 26-28 of copending U.S. application no. 11/781,902.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a generic polypeptide conjugate as defined in claim 1. Claims 8 and 23 indicate that the peptide may be selected from a group that includes erythropoietin. Claims 3, 4, 7 and 27 indicate that the polymeric moiety is poly(ethylene glycol) that is linear or branched, with structures as defined in said claims. Claims 7 and 26 indicate that the polymeric moiety is attached via the sugar residue denoted as formulas (III) or (VII).

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6 and 34 are seen to be obvious over claims 1-8, 10, 23 and 26-28 of copending U.S. application no. 11/781,902.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6-8, 13, 16, 19, 20 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 179-212 of copending U.S. application no. 11/701,949.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a covalent conjugate between an erythropoietin peptide and a water soluble polymer, wherein said water soluble polymer is covalently attached to said erythropoietin peptide at a glycosyl or amino acid residue of said erythropoietin peptide via a first glycosyl linking group. The first glycosyl linking group is a sialic acid residue (claim 186). The water soluble polymer comprises PEG (claim 187-190). The copending application is also drawn to a method of forming a covalent conjugate between EPO peptide and a water soluble polymer wherein the EPO peptide has a glycosyl residue having the formula shown in claim 193.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6-8, 13, 16, 19, 20 and 34 are seen to be obvious over claims 179-212 of copending U.S. application no. 11/701,949.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of copending U.S. application no. 11/867,553.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to a peptide conjugate comprising a peptide which is covalently attached to a moiety which is a member selected from the group as shown in claim 1. Claim 3 defines the PEGylated structures on sialic acid. The peptide is selected from a group that includes erythropoietin (claim 4).

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1 and 34 are seen to be obvious over claims 1-4 of copending U.S. application no. 11/867,553.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 89-136 of copending U.S. application no. 11/714,874.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to an O-linked covalent conjugate of a peptide having the formulas as defined in claims 89, 103, 110 or 115. Claim 125 indicates that the peptide may be selected from a group that includes erythropoietin. Claims 122-124 indicate that the polymeric moiety is poly(ethylene glycol). Claim 112 indicates that the glycosyl linking group is sialic acid. Claim 133 defines the structure of sialic acid modified with the polymeric modifying group PEG.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1 and 34 are seen to be obvious over claims 89-136 of copending U.S. application no. 11/714,874.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6-8 and 13-26 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-51, 54 and 57-73 of copending U.S. application no. 11/440,839.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to an erythropoietin formulation comprising an erythropoietin peptide, wherein the erythropoietin peptide comprise a glycosyl linking group attached to an amino acid residue of said peptide, said glycosyl linking group comprising a modified sialyl residue having the formula as shown in claim 1. The dependent claims further limit the modifying group to various PEG structures and further limit the glycosyl linking group to defined glycosyl structures.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6-8 and 13-26 and 34 are seen to be obvious over claims 1-51, 54 and 57-73 of copending U.S. application no. 11/440,839.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6-8 and 13-26 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 4-47, 50 and 52-81 of copending U.S. application no. 11/144,223.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending application is drawn to an erythropoietin peptide comprising a glycosyl linking group attached to an amino acid residue of said peptide, said glycosyl linking group comprising a modified sialyl residue having the formula as shown in claim 1. The claims are also drawn to a method of preparing the said erythropoietin peptide, as well as methods of treatment of various conditions comprising administration of the said erythropoietin peptide. Claim 26 is drawn to a pharmaceutical formulation comprising the said erythropoietin peptide and a pharmaceutically acceptable carrier.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6-8 and 13-26 and 34 are seen to be obvious over claims 1, 4-47, 50 and 52-81 of copending U.S. application no. 11/144,223.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 12-18, 23-29, 31-69, 72-76 and 78-96 of copending U.S. application no. 10/530,972, which will be issued as U.S. Patent No. 7,696,163 B2 on 13 April 2010.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a glycoPEGylated EPO peptide comprising an EPO peptide and at least one glycan and at least one PEG molecule covalently attached to said glycan, wherein said glycoPEGylated EPO peptide is made by a method comprising adding said PEG molecule to said EPO peptide using a glycosyltransferase. The PEG moiety is linked to at least one sugar moiety selected from the group consisting of fucose, GlcNAc, Gal, and sialic acid. The claims are also drawn to a method of making a glycoPEGylated EPO peptide, as well as to a method of treating various conditions comprising administration of the glycoPEGylated EPO peptide.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1 and 34 are seen to be anticipated by claims 12-18, 23-29, 31-69, 72-76 and 78-96 of copending U.S. application no. 10/530,972, which will be issued as UU.S. Patent No. 7,696,163 on 13 April 2010.

Claims 1, 6-8, 13, 16, 20, 23-26 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-43 of U.S. Patent No. 7,473,680 B2.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a method of forming a covalent conjugate between a water soluble polymer and a glycosylated or non-glycosylated peptide. Claims 41 and 43 indicate that the peptide may be selected from a group that includes erythropoietin. Claims 5-8, 21-23 and 42 indicate that the polymeric moiety is poly(ethylene glycol). Claim 42 further indicates that PEG is conjugated to the glycosyl linking group sialic acid at C-5. Claim 26 defines the structure of sialic acid modified with the polymeric modifying group PEG. Claim 24 defines the structure of PEG that modifies sialic acid.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6-8, 13, 16, 20, 23-26 and 34 are seen to be anticipated by claims 1-43 of U.S. Patent No. 7,473,680 B2.

Claims 1, 6-8, 13, 16, 20, 23-26 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-120 of U.S. Patent No. 7,416,858 B2.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a pharmaceutical composition comprising a pharmaceutically acceptable diluent and a covalent conjugate between PEG and a glycosylated or non-glycosylated peptide, wherein said PEG is conjugated to said peptide via a glycosyl linking group, wherein said glycosyl linking group is interposed between and covalently linked to both said peptide and said PEG. Claims 9, 23 and 40, for example, indicate that the peptide may be selected from a group that includes erythropoietin. Claim 112 indicates that the modified glycosyl moiety, and the glycosyl moiety linking PEG to the peptide, has the structure as in said claim. PEG is conjugated to the glycosyl linking group sialic acid at C-5. Claim 133 defines the structure of sialic acid modified with the polymeric modifying group PEG.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6-8, 13, 16, 20, 23-26 and 34 are seen to be anticipated by claims 1-120 of U.S. Patent No. 7,416,858 B2.

Claims 1, 7, 8, 13-26 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-36 of U.S. Patent No. 7,405,198 B2.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to an EPO peptide comprising a sialic acid moiety having the formula as indicated in the claim. Claims 3-20 and 27-34 further limit the glycosyl moiety of sialic acid conjugated to the peptide, as well as limiting the amino acid residue to asparagine, and the EPO peptide to SEQ ID NO:1. The claims are also drawn to a method of making the PEGylated EPO peptide (claims 21-24) and a method of treating various conditions comprising administration of an amount of the EPO peptide (claims 35 and 36). Claim 26 is drawn to a pharmaceutical formulation comprising the covalent conjugate.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 7, 8, 13-26 and 34 are seen to be anticipated by claims 1-36 of U.S. Patent No. 7,405,198 B2.

Claims 1, 6-8, 13-26 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 7,214,660 B2.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a covalent conjugate between an EPO peptide and PEG, wherein said PEG is covalently attached to said EPO peptide at a preselected glycosyl or amino acid first residue of said EPO peptide via a first intact glycosyl linking group. Claims 10, 18 and 22 further claim a cell-free, in vitro method for forming a covalent conjugate between an EPO peptide and PEG, wherein said EPO peptide comprises a glycosyl residue having a formula as indicated in the said claims. The PEG is selected from linear PEG and branched PEG, wherein said PEG is monomethoxy-poly(ethylene glycol) (claims 24 and 25).

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6-8, 13-26 and 34 are seen to be anticipated by claims 1-32 of U.S. Patent No. 7,214,660 B2.

Claims 1, 6-8, 13, 16, 20, 23-26 and 34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 7,138,371 B2.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a covalent conjugate between PEG and a peptide, wherein said PEG is covalently attached to said peptide at a glycosyl or amino acid residue of said peptide via an intact glycosyl linking group comprising a sialic acid residue covalently linked to said PEG. Claims 14, 19 and 25 indicate that the peptide may be selected from a group that includes erythropoietin. Claims 11, 17 and 24, for example, indicate at which position PEG is conjugated to sialic acid. Claim 26 is a pharmaceutical formulation comprising the covalent conjugate.

The claims of the instant application are drawn to an erythropoietin peptide comprising the moiety as shown in instant claim 1. Claims 6-8 and 13-22 further limits the modifying group present on the conjugate to linear PEG polymers and the glycan structures to N-linked glycans conjugated to the asparagine residue of the polypeptide backbone, as recited in said claims.

Thus, the instant claims 1, 6-8, 13, 16, 20, 23-26 and 34 are seen to be anticipated by claims 1-27 of U.S. Patent No. 7,138,371 B2.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/SCARLETT GOON/
Examiner
Art Unit 1623